EXHIBIT 18

EXPERT REPORT OF MARK A. SCHUMACHER, M.D., Ph.D.

MARCH 25, 2019

73. The daily clinical consequences of the myth of no-ceiling dose is reflected in the increasing number of opioid-dependent patients. What was once unimaginable is now common: to see a patient taking over 500, or even 1,000 MMEs (oral morphine equivalents) daily admitted to our hospital and continue to complain of severe pain. It is a myth that there is no ceiling dose with opioids as illustrated by very real risk and consequences of overdose and death from long-term opioid therapy. Mortality rates increased gradually across the range of average daily milligrams of morphine equivalents indicating a single threshold of harm does not exist. Thus, there are no single inflection points defining a threshold of opioid risk/safety. The situation becomes even more dire if benzodiazepines are taken concurrently. The higher the dose, the higher the risk of death; this risk may occur for some patients at doses that previously were thought to be "safe." (Dasgupta et al. 2016).

74. Other studies have also examined the relationship between long-term opioids and overdose and death. Persons who received 3 or more opioid prescriptions within 90 days for chronic noncancer pain between 1997 and 2005 and received 50 to 99 mg/d of opioids (compared with 1 to 20 mg/d) had a 3.7-fold increase in overdose risk, while patients receiving 100 mg/d or more had an 8.9-fold increase in overdose risk (Dunn et al. 2010). Higher opioid doses were associated with increased risk of opioid overdose death with a maximum prescribed dose of 100 mg/d or more (Bohnert et al. 2011). When the risk of overdose was examined in patients taking a daily dose of less than 20 mg versus those with average daily doses of 200 mg or more of morphine (or equivalent), there was a nearly 3-fold increase in the risk of opioid-related mortality (Gomes et al. 2011). Other patient cohorts have shown even greater risks at a

sales force to meet the goal of "pushing higher doses" with "rewards that increased steeply" for "deeper penetration into the high-strength [Oxy/APAP] market"—defined as Percocet 7.5/325 and 10/325 and all Oxy/APAP 7.5/500 and 10/650 variants (Percocet, Endocet, and Generic Oxycodone/APAP).

threshold of intermediate dosing (>40 morphine milligram equivalents) with an odds ratio of 12.2 (CI 9.2-16.0) (Paulozzi et al. 2012).

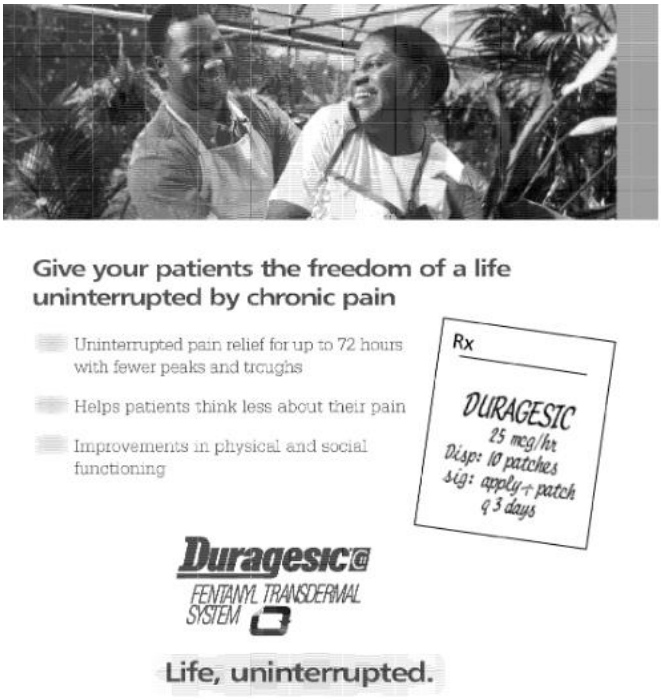
75. Taken together, with more recent studies, it appears that there is no minimum threshold below which risk of harm is zero, and risk generally increases with daily dosing. The notion that taking less than 100 MME / day is somehow safe is not supported by the literature and represents a sobering conclusion that the unnecessary initiation of long-term opioid therapy has the potential of causing great harm at any dose (Zedler et al. 2014; Bohnert et al. 2016).

c. Opioid manufacturers misleadingly represented that chronic opioid therapy improves function and quality of life.

76. Opioids were marketed for years as the panacea for pain that would give patients back their lives. The now notorious 1998 Purdue promotional video featuring Dr. Spanos, "I got my life back," painted a picture of a miracle drug at work. See PKY180989588 (Exhibit A-1.12). Patient brochures and advertisements similarly told people that opioids could improve their health, function and quality of life. Some examples include:

- "Myth: Opioids make it harder to function normally. Fact: When used correctly for appropriate conditions, opioids may make it easier for people to live normally." --- Janssen patient guide, Finding Relief: Pain Management for Older Adults (2008) JAN-MS-00476773 at 10 (Exhibit A-1.21).
- "Multiple clinical studies have shown that long-acting opioids, in particular, are effective in improving: Daily function, Psychological health, Overall health-related quality of life for people with chronic pain." --- American Pain Foundation, *A Policymaker's Guide to Understanding Pain & Its Management* at 29 (2011) (*See* Exhibit A-1.22).
- Purdue 2006 ad for OxyContin, "There can be life with relief": PDD1501614879 at 3 (Exhibit A-1.23).

- JAN-MS-00306286 at 8 (Exhibit A-1.24).



77. The impression created by these materials is that opioids are safe and effective, seldom harmful, and usually beneficial. But opioids—whether formulated as immediate-release or extended-release, and with or without "abuse-deterrent features"—are dangerous and highly

addictive. But that certainly was not the message communicated by Purdue and the other manufacturers. Instead, doctors and patients were told that studies proved that opioids would improve function and enhance quality of life for persons suffering from chronic pain. There was no scientific basis for these statements when made, and abundant evidence developed over time showing that long-term opioid therapy, rather than improving function and quality of life, leads to poor functional outcomes.

78. For example, in a Danish health study, opioid usage was significantly associated with reporting of moderate/severe or very severe pain, poor self-rated health, not being engaged in employment, higher use of the health care system, and a negative influence on quality of life. Put otherwise, opioid treatment of long-term/chronic non-cancer pain does not seem to fulfill any of the key outcome opioid treatment goals: pain relief, improved quality of life and improved functional capacity (Eriksen et al. 2006). In fact, the odds of recovery from chronic pain were almost 4 times higher among individuals not using opioids compared with individuals using opioids (Sjogren et al. 2010). There is also evidence that return to work is more often delayed than expedited for patients on chronic opioids (Von Korff 2013; Franklin et al. 2008; Franklin et al. 2009).

d. Purdue promoted and encouraged confusion about the strength of oxycodone.

79. Physicians were reluctant to prescribe opioids, particularly morphine, because of the stigma. Morphine was a cancer drug, and it was known to be highly addictive. Purdue worked around this problem by taking advantage of confusion about the active ingredient in OxyContin. Purdue knew that physicians often believed oxycodone was less powerful than morphine - when in fact, it was stronger. As explained by Purdue's former CEO Michael Friedman in an email to Richard Sackler on April 22, 1997:

DATED March 25, 2019.

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